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RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE: Ex-vivo Cultivated Limbal Stem Cell Transplantation for Treatment of Superficial Corneal Pathologies.

PROTOCOL N^o: LVPEI-2014-1 Version 1 Dated 15 January 2014

ICF VERSION N^o: 1.0

ICF VERSION DATE: 15-Jan-2014

CO-ORDINATING CLINICAL CENTRE L V Prasad Eye Institute
L V Prasad Marg
Road No. 2, Banjara Hills
Hyderabad, Andhra Pradesh - 500034,
India

**FUNDING SOURCE/
RESEARCH GRANT** L.V. Prasad Eye Institute

INVESTIGATIONAL AGENT Ex-vivo cultivated limbal stromal stem cells

INDICATION Superficial corneas scars following trauma or infectious bacterial/fungal keratitis.

CLINICAL PHASE Phase 1

**NAMES AND AFFILIATIONS
OF INVESTIGATOR (S)** Dr. Sayan Basu
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1. BACKGROUND

Dear Patient,

This consent form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand before making your decision.

After all of your questions have been answered, if you still wish to take part in the study, you will be asked to sign this informed consent form and given a copy of the signed consent form to keep.

2. SPONSOR OF THE STUDY

This is an Investigator-Initiated Study and your doctor has been involved in designing this study. The sponsors for the study are LV Prasad Eye Institute, Hyderabad.

3. PURPOSE

You have been invited to participate in this Research Study because you have blindness in one eye due to corneal opacity either following trauma or infection.

The current standard of care for your condition is surgical excision of the scarred part of the cornea and replacing it with a clear corneal graft from a deceased donor (corneal transplantation, corneal grafting or keratoplasty). There are millions of individuals in the world with similar problems in their eyes. However, there is a huge shortage of donor corneas worldwide, especially in developing countries like India. Moreover, although initially successful, corneal transplantation carries the risk of failing in the long-term because the transplanted cornea is from a different person and your body may react against it (immunological rejection).

Around two decades ago stem cells were discovered in eyes of adult humans, located just around the cornea. These stem cells are capable of regenerating or repairing the surface of the cornea when it is damaged by severe injury like burns. Your doctors have been performing this procedure successfully in patients for the last 13 years. More recently, a different kind of stem cells were discovered in the same location, which are capable of repairing corneal scars and restoring transparency. These cells have been used successfully in the laboratory and in pre-clinical animal models.

This study will attempt to evaluate the safety of using limbal stem cells to treat the corneal scarring that is causing poor vision in our eye.



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4. STUDY PARTICIPANTS

Participants in this study should be aged 18 and 60 years and with corneal scar in one eye following injury or infection.

5. EXPECTED STUDY DURATION AND NUMBER OF PARTICIPANTS

A maximum of 20 patients will participate in this study that lasts for about three months for each patient.

6. STUDY VISITS AND PROCEDURES

During these three months, there will be 8 clinic visits at different intervals. You will be interviewed and will undergo specific diagnostic investigations, to confirm whether you can be selected to be part of this study. If you meet all the entry criteria you will be enrolled to the study. You will undergo two surgical procedures in your blind eye. Limbal Stem cells have been cultured in the laboratory. You will undergo the procedure in which these cells will be transplanted back to your eye (transplantation). You will be admitted and observed as in-patient for a day after surgery and then discharged. You will thereafter be required to visit the clinic at week 1, week 6 and month 3 after your surgical procedure. During these visits your doctor will monitor your post-surgical progress and perform some tests, which are detailed in the section below.

In addition to the requirement of providing written informed consent, audio-visual recording of the informed consent process, including the procedure of your doctor providing information to you on the study and your understanding on the consent, will be done while adhering to the principles of confidentiality. The recording(s) will be used for review of the consent process by the ethics committee and the regulatory authorities. This recording will not be used for any other purpose.

The recordings will be maintained adhering to the principles of confidentiality (restricted access). The recording of the consent process will be archived along with the other study documents until 15 years after the completion of the study.

6.1 Screening Visit

This will be your first visit for the study. You may begin the study only after you have signed this informed consent. After this, you will have a number of routine tests like; Slit lamp biomicroscopy and photography, measure of pressure in the eyes, test for dryness in the eyes and any existing signs and symptoms to confirm you are eligible to participate in the study. These tests will be completed within 60 days of your written agreement to participate in the study.

In case you do not pass the screening procedure, you will not participate in the study.



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6.2 Day 0-Day of Surgery

In case you are found eligible you will be required to come for this visit. On this day of you will be assigned a Unique Patient Identification Number and other pre-surgery investigations will be done. You will undergo the transplantation of stem cells that were recovered from cadaveric sources. You will remain under in-patient care for 24 hours and will be observed and monitored for post-surgical progress and then discharged from in-patient care.

6.3 Day 1 -Post Surgery

There will be a few assessments performed before discharge from hospital; post-surgery your progress will be monitored. Any new signs or symptoms will be recorded. Eligibility to continue on the trial will be reviewed. Detailed ophthalmic examinations will be done. You will be discharged from in-patient care. Your doctor or designated staff will provide appointment for next clinic visit to you.

6.4 Follow-up Visits:

Follow-up Visits will be scheduled at week 1, week 6, and month 3 post-surgery.

During all these visits you must keep your doctor informed of any good or bad experiences you may have in the period between the visits, any changes in the medications you are taking or change in your general health condition.

7. STUDY RESTRICTIONS/PARTICIPANT RESPONSIBILITIES

The following should not be done while you are on the study:

- Undergo any ophthalmic procedure without communicating that to the study doctor
- Enter another clinical trial
- In case you are a female of child-bearing age you should not get pregnant while on the trial. In case you are male, you should exercise effective birth control measures while on trial. In case you do get pregnant or your partner gets pregnant (in the case of male participants), YOU SHOULD INFORM YOUR DOCTOR IMMEDIATELY.

8. SURGICAL PROCEDURE AND ASSOCIATED RISKS

8.1 Surgical Procedure

The surgery will be performed under local anesthesia, which involved giving a small injection around the affected eye. This injection feels like a pinprick. The surgical procedures will take around 15-30 minutes and during this time you have to lie down on the operating table while your eye will be numb and you should not feel any pain. You can talk to the surgeons during the procedures to indicate if you are having any discomfort and they will make sure that you are comfortable. Both procedures are extra-ocular, meaning that it is not necessary to make any opening into the eye and only the surface is touched. Immediately following the surgery your eye will be bandaged overnight.

8.2 Risks and Discomforts:

- The surgical procedures are quick and recovery period involves minimal pain and/or discomfort. You may have some irritation in the eye after the first procedure (limbal biopsy). This usually is very mild and resolves in a day or two after using eye drops.
- There have never been any reports of infection after the limbal biopsy or cultivated limbal stem cell procedure. However, theoretically the risk exists, as it is a surgical procedure.
- It is very unlikely that you will experience a loss of vision.
- You should be able to go back to your everyday routine immediately after the first procedure (limbal biopsy) and one week after your second surgery (transplantation).

9. ASSESSMENTS:

The eye examinations are non-invasive and should not cause any discomfort, but you will need to allow time for these to be completed. All of the tests involved in this study are standard eye assessments; these tests even when done routinely could cause some discomfort for you. However, associated risks and inconveniences are minimal.

Intra-Ocular measurements: The pressure in your eyes will be measured using an instrument known as a tonometer. You will not feel the tonometer on your eye and this procedure is quick and generally painless.

Slit-lamp photography: Photographs of your eyes will be taken at each visit to document the progress of your treatment. This does not cause any discomfort.

Anterior Segment Optical Coherence Tomography (ASOCT): This is a non-contact method of imaging your corneas with infra-red light and is generally painless and takes few minutes for both eyes.

Confocal Microscopy: This is similar to tonometry for recording pressure and will be performed after putting anesthetic drops on your eyes. You will not feel any pain.

10. NEW FINDINGS

You will be told about any new information that might affect your decision to be in this study. You may be asked to sign a revised consent form if this occurs.

11. EXPECTED BENEFITS:

There may or may not be a benefit to you. But the information we get from the study may help us to develop this procedure as substitute to the current standard practice of donor

cornea transplantation, and extend this benefit to other patients as a more convenient and more cost effective option, and to others who are waiting for transplantation due to a severe shortage or good quality donor corneas.



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12. COSTS

There will be no additional cost to participate in this study. All procedures and visits are not charged.

Travel expenses will be paid at a maximum of Rs. 1000/-per visit (Rupees One thousand only) or on a pro rata basis.

In case of study related injury or death, LV Prasad Eye Institute will provide complete medical care free of charge along with compensation for the injury or death to you or your nominee as decided by the Ethics Committee and the Regulatory Authority.

13. ALTERNATIVES TREATMENT:

You may discuss with the investigator for the alternative treatment available to you as a patient.

14. CONFIDENTIALITY

The monitor(s), the auditor(s), the Ethics Committee and the regulatory authority (ies) will be granted direct access to your original medical records for verification of clinical trial procedures and/or data. This would be done without violating your confidentiality as a participant, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, you as a participant or your legally acceptable representative is authorizing such access.

Your personal identity, that is your name, address, and other identifiers, will be kept confidential. You will have a code number and your actual name will not be used. Only your study doctor will be able to link the code number to your name and will keep this information for 15 years.

Your information will be used in the following ways:

- to do the research,
- to study the results, and
- to make sure that the research was done right.

15. VOLUNTARY PARTICIPATION:

Your participation in the trial is entirely voluntary and you may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which you may be otherwise entitled.

There may be certain unforeseeable circumstances and/or reasons under which your participation in the trial may be terminated. The investigator may discontinue your participation from the study treatment at any time for any of the following reasons:



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- If you suffer from any adverse event that, in the judgment of your study doctor presents an unacceptable consequence or risk to you;
- If you show significant protocol non-compliance or fail to receive the appropriate amount of the study medication/therapy;
- If you refuse to continue medication/therapy for any reason.

16. RESPONSIBILITIES OF A PARTICIPANT:

- Inform the site personnel about your correct medical history, including all your health problems that you have suffered from - in the past or may be currently suffering from along with the medications that you are currently consuming;
- Visit the site personnel at the timelines that you are requested to do so;
- Inform the site personnel about any desirable/undesirable effects that you may face during the study treatment phase;
- The aspects of the trial that are experimental have been explained to you, for further details you may feel free to discuss with your investigator.
- Obtain a copy of this signed informed consent and keep it safely with you.

17. CONTACT INFORMATION:

For questions about your rights as a study patient, you may contact the Ethics Committee Member, **Dr. Harsha B.L. Rao, Member Secretary on 040-30612620**

For questions about the study, you may call the study doctor:

Dr. Sayan Basu: +91 9989479969

Dr. Virender S Sangwan: +91-9849294656

By signing this document, you are in no way waiving your legal rights or releasing the investigator / institution / site personnel and Sponsor from their legal and professional responsibilities.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.



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STATEMENT OF CONSENT FORM

Study Title: Autologous Ex-vivo Cultivated Limbal Stem Cell Transplantation for Treatment of Superficial Corneal Stromal Scars: A Pilot Study

Protocol Number: LVPEI-2013-11

Participant's Name	
Participant's Initials and Screening Number	
If enrolled then Unique Patient Identification Number (UPIN)	
Address and Contact number of the participant	
Occupation and qualification of the Participant	
Annual income of the participant	
Date of Birth / Age	
Name of Nominee provided by trial participant	
Relationship of nominee to the trial participant	
Address and contact number of the nominee	

By signing below, I show that:

Please initial box
(Participant)

- (i) I confirm that I have read and understood the information mentioned in this Information and Consent Form Version 1.0 Dated _____ for the above study, its contents were explained to me and have had the opportunity to ask questions. The study doctor or study staff has talked with me about this study. All of my questions were answered to my satisfaction.

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- (ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. []

- (iii) I understand that the Sponsor (LV Prasad Eye Institute) of the clinical trial, others working on Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. []

- (iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s) []

- (v) I have had time to make my decision whether or not to take part in this research. I agree to take part in the research study described in this form. I will receive a signed and dated copy of this form for my records. []

SIGNATURES SECTION:

1. Participant:

Name of the Participant/Legally Acceptable Representative:	
Signature or (Thumb impression) of the Participant/Legally Acceptable Representative	
Date	

2. Investigator:

To the best of my ability, I have explained and discussed the full contents of the study, including all of the information contained in this consent form. All questions of the research participants have been accurately answered.

Name of the Investigator or Authorized Study Team Member administering consent:	
Signature of the Investigator or Authorized Study Team Member administering consent:	
Date	



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3. WITNESS STATEMENT (OPTIONAL)

If this consent form is read to the participant because the participant is unable to read the form, an impartial witness not affiliated with the research or investigator must be present for the consent and sign the following statement:

As an impartial third party, I witnessed the entire consent discussion and the participant's signature (or Thumb impression) on this form. I attest that this entire form was read to the participant named above. This person had enough time to consider this information, had an opportunity to ask questions, and voluntarily agreed to be in this study:

Name of the Impartial Witness	
Signature of Impartial Witness	
Date	

(Copies of the patient information sheet and duly filled informed consent form with signatures of all parties shall be handed over to the participant or his/her attendant also.)